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# One Hundred Nine Living Donor Liver Transplants in Adults and Children: A Single-Center Experience

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**Objective**

To summarize the evolution of a living donor liver transplant program and the authors' experience with 109 cases.

**Summary Background Data**

The authors' institution began to offer living donor liver transplants to children in 1993 and to adults in 1998.

**Methods**

Donors were healthy, ages 18 to 60 years, related or unrelated, and ABO-compatible (except in one case). Donor evaluation was thorough. Liver biopsy was performed for abnormal lipid profiles or a history of significant alcohol use, a body mass index more than 28, or suspected steatosis. Imaging studies included angiography, computed tomography, endoscopic retrograde cholangiopancreatography, and magnetic resonance imaging. Recipient evaluation and management were the same as for cadaveric transplant.

**Results**

After ABO screening, 136 potential donors were evaluated for 113 recipients; 23 donors withdrew for medical or personal reasons. Four donor surgeries were aborted; 109 transplants were performed. Fifty children (18 years or younger) received 47 left lateral segments and 3 left lobes; 59 adults received 50 right lobes and 9 left lobes. The average donor hospital stay was 6 days. Two donors each required one unit of banked blood. Right lobe donors had three bile leaks from the cut surface of the liver; all resolved. Another right lobe donor had prolonged hyperbilirubinemia. Three donors had small bowel obstructions; two required operation. All donors are alive and well. The most common indications for transplant were biliary atresia in children (56%) and hepatitis C in adults (40%); 35.6% of adults had hepatocellular carcinoma. Biliary reconstructions in all children and 44 adults were with a Roux-en-Y hepaticojejunostomy; 15 adults had duct-to-duct anastomoses. The incidence of major vascular complications was 12% in children and 11.8% in adult recipients. Children had three bile leaks (6%) and six (12%) biliary strictures. Adult patients had 14 (23.7%) bile leaks and 4 (6.8%) biliary strictures. Patient and graft survival rates were 87.6% and 81%, respectively, at 1 year and 75.1% and 69.6% at 5 years. In children, patient and graft survival rates were 89.9% and 85.8%, respectively, at 1 year and 80.9% and 78% at 5 years. In adults, patient and graft survival rates were 85.6% and 77%, respectively, at 1 year.

**Conclusion**

Living donor liver transplantation has become an important option for our patients and has dramatically changed our approach to patients with liver failure. The donor surgery is safe and can be done with minimal complications. We expect that living donor liver transplants will represent more than 50% of our transplants within 3 years.

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The shortage of cadaveric organs for liver transplantation has limited our ability to provide this life-saving therapy.[1] Historically, the shortage was most profound for children, who require smaller grafts. The innovative techniques of reduced-size and split liver transplantation relieved this shortage to some extent, allowing children greater access to transplants. Raia et al[2] and Broelsch et al[3] extended these techniques, resecting left lateral segments from living adults

for transplantation into children. Pediatric living donor liver transplantation (LDLT) with left lateral segment grafts (segments 2 and 3) has nearly eliminated waiting list deaths among children and has improved graft and patient survival rates.[4,5] Further, waiting times for pediatric cadaveric livers are dramatically shorter. LDLT in children is associated with minimal donor complications.[3,6,7]

Adults waiting for liver transplant face similar challenges to those faced by children before LDLT became routine.[8] Nearly 10% of patients on our waiting list die; the national liver transplant waiting list death rate in 1999 was 8.3%.[1] In 1998, we began to offer LDLT to adult recipients. Here we summarize our experience with 109 LDLTs in children and adults.

## METHODS

Between August 1988 and October 2000, 1,629 patients underwent 1,916 liver transplants, including 201 cases in children (age 18 or younger). Our pediatric LDLT program was initiated in 1993; since then, 50 children have received living donor grafts. In 1998, we expanded the program to larger children and adults, initially using left lobe grafts ($n = 9$) and then right lobes ($n = 50$). Overall, living donors have been used for 109 (5.7%) transplants.

### Donors

Healthy individuals ages 18 to 60 years could be considered as donors. Evaluation consisted of a complete medical and psychosocial history and physical examination.[9] A physician not involved in care of the recipient, who could be an unbiased advocate for the donor, carried out donor evaluations. At multiple points during the evaluation, the risks and benefits of the procedure were explained. Donors were also evaluated to assess altruism and possible coercion and were informed that they could withdraw at any time.

The initial biochemical evaluation included viral serologies and blood type. Only ABO identical or compatible donors were considered, except for one emergent pediatric transplant for fulminant hepatic failure in which a mismatched donor was used. When indicated, cardiology and/or psychiatry clearances were obtained. For early cases, imaging studies included angiography, computed tomography (CT), and endoscopic retrograde cholangiopancreatography. Later, most patients were evaluated with CT and/or magnetic resonance imaging, with hepatic volumetry and vascular reconstructions. As we gained experience, magnetic resonance imaging replaced all preoperative imaging except for intraoperative cholangiography (still used to define biliary anatomy). Graft volume was estimated before surgery by CT scan or magnetic resonance imaging and measured after back-table flush.

Liver biopsies were performed for abnormal lipid profiles or history of significant alcohol use, body mass index (BMI) more than 28, or imaging studies suggestive of steatosis. Donors with more than 25% steatosis were excluded. When the evaluation was completed, the case was submitted to a multidisciplinary committee for approval. One unit of autologous blood was stored for each donor.

Donor demographics, relationship to the recipient, surgical details, postoperative biochemical profiles, complications, and outcome were analyzed.

### Recipients

The evaluation and the management of patients were the same as for cadaveric transplantation.[9] Once the decision to proceed with transplantation was made, the option of LDLT was discussed with the patient and family at length, or with the parents in pediatric cases. In general, adults offered LDLT were United Network for Organ Sharing (UNOS) status 2B or 3 undergoing primary transplantation.

Recipient demographics, indication for transplant, UNOS status, Child-Pugh score (adults only), surgical details, graft/recipient weight ratio (GRWR),[10] primary immunosuppression, posttransplant biochemical profiles, surgical complications (including incidence of small-for-size syndrome[10]), and patient and graft survival were analyzed.

### Donor Operations

For left lateral segmentectomy, we followed the technique of Broelsch et al.[3] After complete left hepatic artery and portal vein dissection, the bile duct or ducts were sharply transected at the edge of the graft and parenchymal transection was initiated just to the right of the falciform ligament and extended down to the hilar plate.

Left lobectomy was performed as described by Broelsch et al,[3] Tanaka et al,[11] and Otte et al.[12] After cholecystectomy and cystic duct cholangiography, the hilar dissection was performed. The bile duct was transected sharply and parenchymal transection was performed, preserving the confluence of the middle and left hepatic veins with the donor left lobe.

For right lobectomy, cholecystectomy and cholangiography were performed as described above. After mobilization of the right lobe, the right hepatic artery was exposed only to the right of the common bile duct. The right portal vein was isolated. The hilar plate was lowered and the right bile duct or ducts were divided sharply. The retrohepatic cava was then dissected, isolating the right hepatic vein and preserving any significant (i.e., diameter $>5$ mm) short hepatic veins for reimplantation. Transection was done with both electrocautery and the Cavitron Ultrasonic Aspirator (CUSA Excel; Valleylab, Boulder, CO), without the use of inflow occlusion. Initially, we attempted to keep the transection plane approximately 0.5 cm to the right of the middle hepatic vein, ligating multiple tributaries to segments 5 and 8. Since our 31st right lobe case, however, the parenchymal transection plane was kept immediately adjacent to the right border of Cantlie's line (middle hepatic vein), allowing the major segment 5 and 8 tributaries to be isolated at their base, before intralobar branching (Fig. 1).

These significant segment 5 and/or 8 hepatic vein tributaries were then preserved and reconstructed to provide optimal graft venous outflow and were anastomosed directly to the recipient middle hepatic vein or inferior vena cava using interposition grafts when necessary.

In all cases, after removal the graft was immediately flushed with cold University of Wisconsin (UW) solution and prepared for implantation. In the case of right lobe grafts, venous reconstructions were performed on the backtable using interposition vein grafts (Fig. 2).

## Recipient Operations

### *Left Lateral Segment/Left Lobe*

After hepatectomy with caval preservation, the graft was implanted in a piggyback fashion, either to extended orifices of the right, middle, and left hepatic veins in children or to the orifices of the middle and left hepatic veins in adults.[13,14] A microscope was used for arterial anastomoses in most pediatric cases. Biliary reconstructions were performed with a Roux-en-Y limb. In children in whom a large graft might be compressed by abdominal closure, vascular inflow and outflow were assessed with ultrasound before and after abdominal closure.

### *Right Lobe*

Hepatectomy was performed with caval preservation. The openings of the left and middle hepatic veins were oversewn unless the middle hepatic vein was needed as a conduit for a significant segment 5 or 8 tributary reconstruction (see Fig. 2). To ensure optimal graft outflow, the right hepatic vein orifice was enlarged by making a caudal extension onto the inferior vena cava. Venovenous bypass was used at the surgeon's discretion. The donor portal vein was anastomosed to the recipient's right or main portal vein, depending on the alignment and size match. Arterial anastomoses were completed between the donor hepatic artery and the recipient right, left, or proper hepatic artery in most cases.

Biliary reconstruction was individualized. Duct-to-duct anastomosis with T tube was used when technically favorable. Most often, Roux-en-Y hepaticojejunostomy was used. Multiple ducts near each other were reconstructed as a single duct anastomosis by suturing the opposing duct sidewalls together. In the event of multiple noncombinable ducts or ducts with significant size discrepancy with the recipient common bile duct, a Roux-en-Y limb was constructed for biliary enteric drainage. Initially, internal and/or external stents were used when reexploration for bile leaks was needed. Subsequently, stents were used routinely, when possible.

## Statistical Analysis

Values are shown as mean ± standard deviation, range, or percentage. Data were analyzed with chi-square, *t* test, and analysis of variance. Kaplan-Meier and log rank for survival comparisons were performed using SPSS for Windows (Release 9.0.1, Microsoft Corp., Redmond, WA). *P* values $< .05$ were considered significant.

# RESULTS

## Donors

After initial ABO screening, 136 potential donors were evaluated for 113 recipients. Fourteen potential donors were medically declined, six refused for personal reasons, and three were declined for size mismatch. Four donor surgeries were aborted; 109 LDLTs were performed. Donor age, gender, and relationship to recipients are shown in Table 1. Overall mean donor body weight was 74.8 ± 15.3 kg. Forty-two donors for adults had a BMI less than 28; 17 were more than 28. In the latter group, 12 had mild (<10%) microvesicular and/or macrovesicular steatosis on biopsy. In seven patients with BMI less than 28, imaging studies suggested fatty liver infiltration, but biopsy showed mild or no fat, and all proceeded with donation.

In right lobe donors, mean lab values on postoperative day 1 were hematocrit, 33.6 ± 5.24%; total bilirubin, 2.34 ± 1.21 mg/dL; aspartate aminotransferase (AST), 275.8 ± 126.8 IU; and prothrombin time, 15.5 ± 2.3 seconds. By postoperative day 3, these values were hematocrit, 30.5 ± 4.34%; total bilirubin, 2.16 ± 1.34 mg/dL; AST, 166 ± 105.8 IU; and prothrombin time, 13.6 ± 1.9 seconds. Test results in left lateral segment and left lobe donors returned to normal by postoperative day 3 (data not shown). One right lobe donor and one left lateral segment donor each required one unit of banked blood.

Left lobe donors had no significant surgical complications. Right lobe donors had three bile leaks (5.1%) from the cut surface of the liver in the immediate postoperative period; these were managed conservatively as controlled fistulas and resolved within 6 weeks. Another right lobe donor had prolonged transient hyperbilirubinemia. Cholangiogram and CT scan showed a bile duct to segments 2/3 to be obstructed, while the duct from segment 4 was separate and patent. With conservative management, the hyperbilirubinemia resolved completely and the patient remains clinically well, albeit with an elevated alkaline phosphatase level.

Two right lobe donors and one left lateral segment donor were readmitted with small bowel obstructions. One recovered with conservative management; the other two required laparoscopic lysis of adhesions. Ten donors developed wound infections; all were treated conservatively.

All donors are alive and well. Their average hospital stay was 6 days.

An additional four donor operations were initiated and aborted (two children, two adults). One pediatric recipient undergoing retransplantation for chronic rejection and profound pruritus was found at exploration to have a significant and remediable bile duct stricture that accounted for his symptoms. The donor operation was aborted before any hepatic dissection. In the second pediatric case, the baby had Alagille syndrome. On hilar dissection in the donor (the

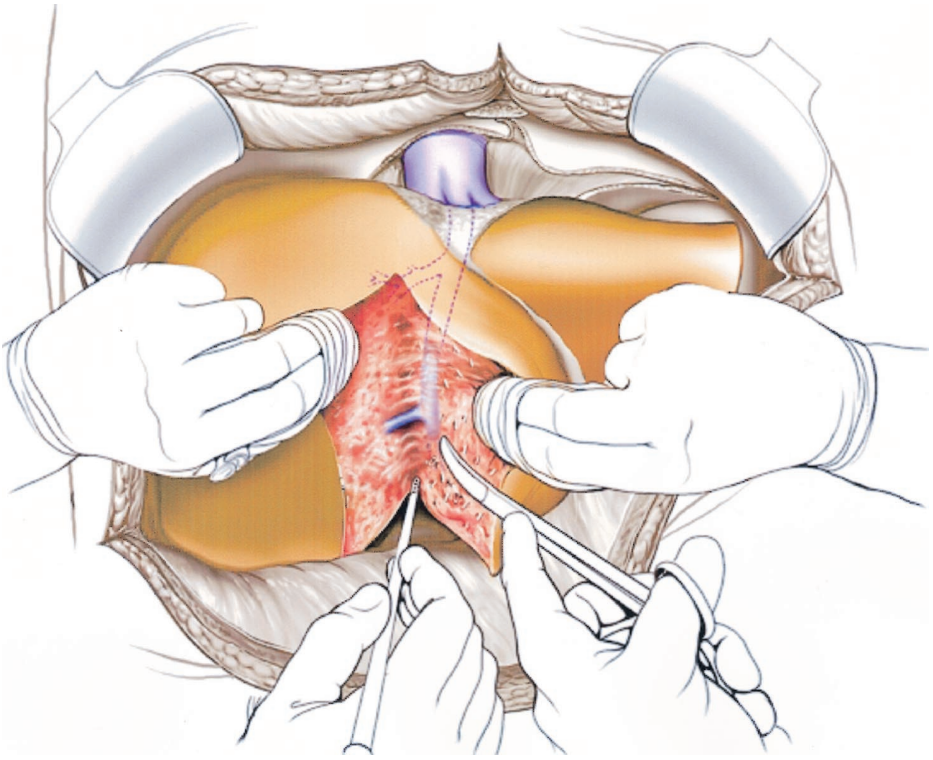

**Figure 1.** Parenchymal transection plane for left and right lobe donors.

mother), the bile duct was found to be less than 1 mm in diameter, inadequate for transplantation. The recipient operation had not yet begun; the donor surgery was aborted after segmental removal. In another adult case, the recipient (with metastatic neuroendocrine replacement of the liver) bled from the right hepatic vein and died during surgery. The donor operation was aborted before any dissection. In the final case, the donor's liver was found on visualization

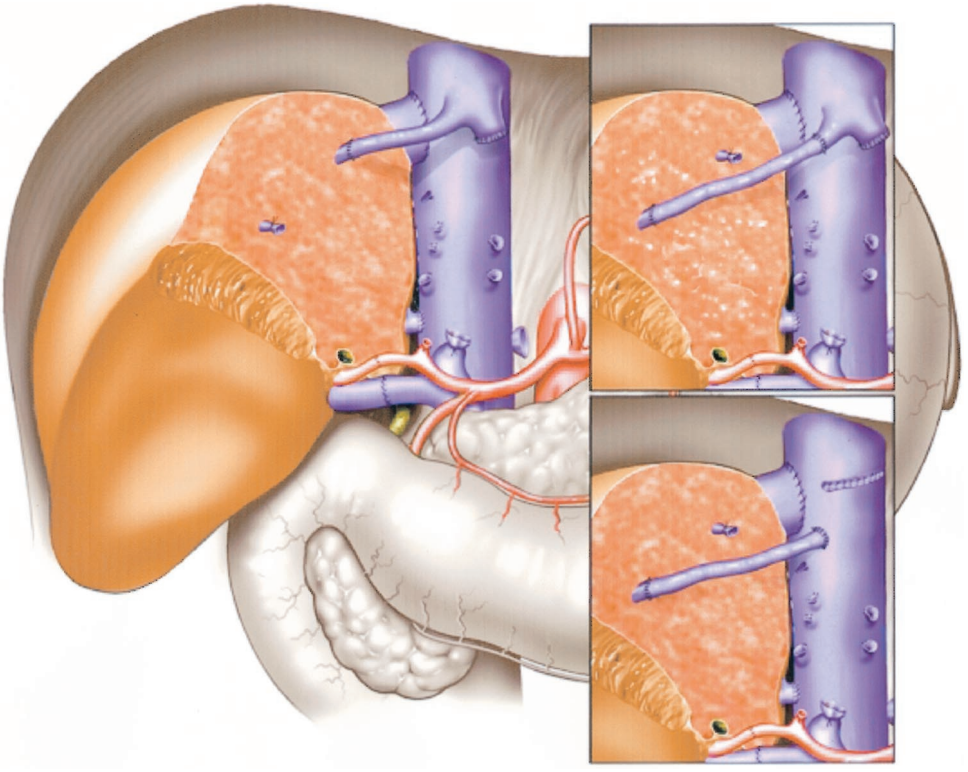

**Figure 2.** Venous reconstructions of significant short hepatic and segment 5 and 8 tributaries.

**Table 1. DONOR DEMOGRAPHICS**

| | Overall | Pediatric (n = 50) | Adult (n = 59) |
|---|---|---|---|
| Age (mean) | 35 ± 9.3 yr (range 19–59) | 32 ± 8.1 yr | 37.9 ± 9.6 yr |
| Gender | 58 males (53.2%)<br>51 females (46.8%) | 21 males (42%)<br>29 females (58%) | 37 males (62.7%)<br>22 females (37.3%) |
| Relationship | 92 related (84.4%) | 48 related (96%)<br>• 27 mothers (54%)<br>• 18 fathers (36%)<br>• 1 grandmother (2%)<br>• 2 aunts (4%) | 45 related (76.3%)<br>• 1 mother (1.7%)<br>• 3 fathers (5.1%)<br>• 15 siblings (25.4%)<br>• 21 children (35.6%)<br>• 1 nephew (1.7%)<br>• 4 nieces (6.8%) |
| | 17 unrelated | 2 unrelated (4%)<br>• 1 stepfather (2%)<br>• 1 friend (2%) | 14 unrelated (23.7%)<br>• 3 spouses (5.1%)<br>• 3 in-laws (5.1%)<br>• 8 friends (13.6%) |

to be swollen; intraoperative echocardiography revealed right ventricular dysfunction. The operation was aborted before the recipient surgery had begun. The donor was later found to have cocaine in his urine.

## Recipients

Living donor grafts were used in 59 adults and 50 children (63 men and boys [57.8%]). Children (mean age 2.4 ± 2.9 years; range 0.5–12; 30 boys [60%]) received 47 left lateral segments and 3 left lobes. Adults (mean age 51.8 ± 12.8 years; range 20–74; 34 men [57.6%]) received 9 left lobes and 50 right lobes. Mean body weight was 10.2 ± 8.5 kg in pediatric recipients and 71.1 ± 12.9 kg in adult recipients.

The most common indication for transplantation in children was biliary atresia (56%) (Table 2). Hepatitis C was the most common indication in adults (40%); 52.2% of patients with hepatitis C also had hepatocellular carcinoma (HCC). Overall, 35.6% of adult recipients had HCC.

Ten patients (9.2%; all children) were UNOS status 1, 1 (0.9%) was status 2A, 40 (36.7%) were status 2B, 37 (33.9%) were status 3, and 21 (19.3%) had not been listed at the time of transplantation. Among adult recipients, 22% were Child-Pugh class A, 50% were Child-Pugh B, and 28% were Child-Pugh C.

Posttransplant biochemical profiles are presented in Table 3.

### *Graft/Recipient Weight Ratio*

Mean measured graft volume was 258 ± 69 g in pediatric recipients and 778 ± 224 g in adult recipients. In the 47 children who received left lateral segments, mean graft/recipient weight ratio (GRWR) was 3.61 ± 2.34% (range 0.74–12.9%). In the three pediatric left lobe recipients, GRWRs were 0.9, 1.52, and 2.25. In the nine adult left lobe recipients, mean GRWR was 0.69 ± 0.20% (range 0.52–1.1%). In the 50 adult right lobe recipients, mean GRWR was 1.18 ± 0.31% (range 0.59–2.15%). The difference in GRWR between adults who received left lobes and those who received right lobes was highly significant ($P = .001$).

### *Surgical Details*

Venovenous bypass was used in 34 adults and in no children. Vascular reconstructions are detailed in Table 4. Preservation and reconstruction of significant middle hepatic vein tributaries was performed in 10 of our final 20 right lobe cases.

Each of the three left lobes given to pediatric recipients

**Table 2. PRIMARY DIAGNOSES**

| | n | With Concomitant HCC (n) |
|---|---|---|
| Pediatric Diagnoses | | |
| Biliary atresia | 28 | — |
| Metabolic liver disease* | 5 | — |
| Cholestatic† | 3 | — |
| Autoimmune | 1 | — |
| Idiopathic | 13 | — |
| Adult Diagnoses | | |
| Hepatitis C | 24 | 13‡ |
| Cryptogenic cirrhosis | 9 | 1 |
| Primary biliary cirrhosis | 7 | 1 |
| Hepatitis B | 6 | 6 |
| Autoimmune hepatitis | 4 | — |
| Primary sclerosing cholangitis | 3 | — |
| Alcoholic liver disease | 2 | |
| Budd-Chiari syndrome | 1 | — |
| Hemochromatosis | 1 | 1 |
| Metastatic tumors | 2§ | — |

* Hyperoxaluria, glycogen storage disease, histiocytosis, Wilson's disease.
† Ductal plate malformation, Alagille's syndrome, primary biliary cirrhosis.
‡ With concomitant alcoholic liver disease.
§ Leiomyosarcoma, 1; neuroendocrine, 1.

**Table 3. RECIPIENTS' POSTTRANSPLANT BIOCHEMICAL PROFILES**

| | Left Lateral Segment (n = 47) | Left Lobe (n = 12) | Right Lobe (n = 50) |
|---|---|---|---|
| Direct bilirubin (mg/dL)* | 3.51 ± 2.0 | 6.25 ± 7.0 | 5.1 ± 4.4 |
| SGOT (IU)† | 1,219 ± 2,480 | 378 ± 238.1 | 515 ± 493.7 |
| SGPT (IU)† | 974 ± 1373 | 320 ± 268 | 537 ± 515 |
| Prothrombin time (sec)* | 17.6 ± 4.4 | 17.7 ± 3.5 | 18.6 ± 23 |
| BUN (mg/dL)* | 22 ± 19.8 | 23.6 ± 11.2 | 61.5 ± 26.1 |
| Creatinine (mg/dL)* | 0.5 ± 0.5 | 0.6 ± 2 | 1.9 ± 0.9 |
| Albumin (g/L)* | 3 ± 0.7 | 3 ± 0.8 | 2.8 ± 0.7 |

Test results available from 34 left lateral segment recipients, 10 left lobe patients, and 45 right lobe patients.
* 48 hours after transplant.
† Peak value in first week after transplant.

had a single bile duct. Among the 47 left lateral segments, 38 (80.9%) had a single bile duct and 9 (19.1%) had two ducts. All biliary reconstructions in children were done with a Roux-en-Y hepaticojejunostomy. The nine adult left lobe grafts all had single bile ducts. Of the 50 right lobe grafts, 21 (42%) had a single bile duct, 23 (46%) had two ducts, 3 (6%) had three ducts, and 1 (2%) had four ducts (data on two grafts not available). Fifteen adults (25.4%) had duct-to-duct anastomoses. Forty-four cases (74.6%) were done with a Roux-en-Y hepaticojejunostomy. Stents were used in 28 cases (56%).

The mean total ischemic time for all LDLTs was 96 ± 102 minutes. Mean cold ischemic time was 55 ± 101 minutes; mean warm ischemic time was 41 ± 12 minutes. There were no significant differences in ischemic times between left lateral segment, left lobe, and right lobe cases.

Adult recipients required a mean of 11 ± 10.3 units of packed red blood cells (250 mL/unit). Pediatric recipients required a mean of 2.3 ± 1.6 units (10 mL/kg/unit).

### *Immunosuppression and Rejection*

Primary immunosuppression was with tacrolimus and steroids in all adults and in most children. (Before the introduction of tacrolimus, cyclosporine-based immunosuppression was used.) Seventeen right lobe recipients also received induction with daclizumab or basiliximab. The incidence of biopsy-proven acute cellular rejection was 18% in adults and 32% in children. All were successfully treated.

### *Complications*

Seven (14%) children had significant bleeding after surgery. In two, bleeding from the cut surface of the graft was found at reexploration. In another, no specific source of bleeding was identified at exploration. The other four were bleeding from the Roux-en-Y enteroenterostomy and were managed endoscopically. Two (4%) left lateral segment recipients had fascial dehiscence; both were primarily repaired. Four (8%) children had intestinal leaks. Three (6%) were reexplored for enteric leaks from the Roux-en-Y enteroenterostomy and one (2%) for an idiopathic small bowel perforation; all were repaired primarily. In addition, two (3.4%) adults had intestinal leaks. One developed a leak from the Roux-en-Y enteroenterostomy and the other had an idiopathic small intestinal perforation, both repaired primarily.

The incidence of major vascular complications was 12% in pediatric patients and 11.8% in adult recipients (Table 5).

Pediatric patients had three bile leaks (6%) and six (12%) biliary strictures. Adult patients had 14 (23.7%) bile leaks and 4 (6.8%) biliary strictures. In the 30 cases in which one bile duct was anastomosed, there were five bile leaks. In the 26 cases with two or more bile ducts, nine patients had leaks.

Small-for-size syndrome developed in four adult recipients of left lobe grafts (44%), in whom the mean GRWR was 0.59%. These patients presented early after transplant with intractable ascites and severe cholestasis despite normalized transaminases. Three underwent retransplantation; two survived. The fourth died of sepsis 4 months after transplant. Two right lobe recipients developed significant congestion of the anterior segments (5 and 8) of their grafts, presenting during the first 2 weeks after the transplant as functional small-for-size syndrome despite GRWRs of 0.79% and 1.46%. Both survived retransplant.

### *Graft Loss and Death*

Three children lost left lateral segment grafts: one to poor early graft function on postoperative day 19, one to veno-occlusive disease resulting from sickle cell disease on postoperative day 117, and one to chronic rejection at 4 years. All underwent cadaveric retransplant; two are alive. Eight adults lost two left lobe and six right lobe grafts: two to mycotic aneurysm (postoperative day 22 and 37), one to hepatic artery thrombosis on postoperative day 40, and five to functional small-for-size syndrome on postoperative day 2, 2, 8, 13, and 16. All underwent cadaveric retransplant; six are alive.

Sixteen recipients died (14.7%; 6 children, 10 adults). Causes of death in the children were sepsis at 12 days, 1 month, and 58 months after surgery (n = 3), posttransplant

lymphoproliferative disease 6 months after surgery (n = 1), cerebrovascular accident (aspergillosis) 1 month after surgery (n = 1), and brain death (n = 1) in a patient who did not recover neurologically after transplant for fulminant hepatic failure. Four adult left lobe recipients died: two of sepsis and small-for-size syndrome (one after retransplant), one with recurrent neuroendocrine tumor 16 months after the transplant, and one of recurrent leiomyosarcoma 19 months after the transplant. Six right lobe recipients died: four of sepsis on postoperative day 16, 26, 37, and 57, one of cardiac arrest on postoperative day 1, and one of recurrent HCC 5 months after the transplant.

### *Survival*

Overall actuarial patient and graft survival rates were 87.6% and 81%, respectively, at 1 year and 75.1% and 69.6% at 5 years (Fig. 3). In children, patient and graft survival rates were 89.9% and 85.8%, respectively, at 1 year and 80.9% and 78% at 5 years (Fig. 4). In adults, patient and graft survival rates were 85.6% and 77%, respectively, at 1 year. One-year patient and graft survival rates were 78% and 55.5%, respectively, for adult left lobe recipients and 85% and 81%, respectively, for right lobe recipients. When 1-year survival was compared between adults with right lobes and those with left lobes, there was a significant difference in graft survival ($P = .02$) but not patient survival ($P = .3$).

## DISCUSSION

Our LDLT program was developed in two phases: children and adults. Both were preceded by careful planning, with approval by the Ethics Committee and Medical Board. We showed both a need for the procedure (in terms of waiting list complications and deaths) and the experience in hepatobiliary surgery and transplantation necessary to perform these procedures safely. Critical to success was ensuring that adequate medical and surgical staff and operating rooms were available for simultaneous donor and recipient operations.

At first, only close family members were allowed to donate. When we offered LDLT to adult patients, unrelated individuals (e.g., spouses, in-laws, close friends) began to step forward and receive consideration. In all cases, we insisted that the donor be healthy, with normal liver function and no comorbidities. Further, we took great care to ensure that donors were acting with full understanding of the risks and benefits for themselves and their recipients and were proceeding of their own free will.

Donor safety is paramount and the donor evaluation is thorough.[15,16] Radiologic imaging of donors' vascular and biliary anatomy is not used to screen donors but as a road map to careful and safe surgery. Clearly, however, two of the four donors whose operations were aborted must be considered errors in evaluation.

**Table 4. VASCULAR RECONSTRUCTIONS**

| | Left Lateral Segment (n = 47) | Left Lobe (n = 12) | Right Lobe (n = 50) |
|---|---|---|---|
| Hepatic artery | Left hepatic artery to:<br>• Proper hepatic artery, n = 9<br>• Right hepatic artery, n = 17<br>• Left hepatic artery, n = 8<br>• Common hepatic artery, n = 7<br>• Other, n = 4<br>Saphenous vein graft to:<br>• Splenic artery, n = 1<br>• Infrarenal aorta, n = 1 | Left hepatic artery to:<br>• Proper hepatic artery, n = 10<br>• Common hepatic artery, n = 1<br>• Saphenous vein graft to the splenic artery, n = 1 | Right hepatic artery to:<br>• Proper hepatic artery, n = 23<br>• Right hepatic artery, n = 17<br>• Left hepatic artery, n = 3<br>• Common hepatic artery, n = 3<br>• Saphenous vein grafts, n = 4 |
| Portal vein | Left portal vein to main portal vein, n = 47 | Left portal vein to main portal vein, n = 12 | Right portal vein to:<br>• Main portal vein, n = 45*<br>• Right portal vein, n = 4<br>• Anterior and posterior right portal veins using a bifurcated iliac vein graft, n = 1 |
| Short hepatic veins | — | — | Direct to inferior vena cava, n = 12† |
| Segment 5 or 8 hepatic veins | — | — | Segment 5 or 8 hepatic veins to:<br>• Middle hepatic vein, n = 1<br>• Middle hepatic vein with saphenous or inferior mesenteric vein interposition graft, n = 6<br>• Inferior vena cava, n = 4 |

* 2 required thrombectomy at transplant.
† In 9 patients; 3 each had 2 accessory veins, and 6 each had 1.

**Table 5. MAJOR VASCULAR AND BILIARY COMPLICATIONS**

| | Left Lateral Segment (n = 47) | Left Lobe (n = 12) | Right Lobe (n = 50) |
|---|---|---|---|
| | | **Vascular Complications** | |
| Hepatic artery thrombosis | n = 2 (4%)<br>• 1 diagnosed on routine ultrasound successfully treated with thrombectomy<br>• 1 diagnosed on postoperative 8, not treated at that time; 2 yr later patient had a biliary stricture that was stented | n = 2 (22.2%; both adults)<br>• 1 underwent retransplant and survived<br>• 1 underwent retransplant but died of sepsis | n = 2 (4%)<br>• 1 underwent retransplant and survived<br>• 1 underwent thrombectomy 16 hr after transplant but died of sepsis 5 mo later |
| Mycotic hepatic artery aneurysms after bile leak | | n = 1 (11%; adult)<br>• Underwent retransplant and survived | n = 1 (2%)<br>• Died of sepsis |
| Hepatic artery stricture | | | n = 1 (2%)<br>• Diagnosed immediately after surgery; successfully treated with balloon dilatation |
| Portal vein thrombosis | n = 3 (6%)<br>• All diagnosed immediately after surgery and successfully treated with thrombectomy | | |
| Venoocclusive disease | • In a patient with sickle cell disease; patient died after retransplant | | |
| | | **Biliary Complications** | |
| Bile leaks | n = 3 (6.4%)<br>• All managed surgically | n = 3 (25%; all adults)<br>• All leaks were from Roux-en-Y hepaticojejunostomy and were managed surgically | n = 11 (22%)<br>• 2 from the cut surface<br>—1 managed conservatively and recovered uneventfully<br>—1 underwent reexploration and recovered uneventfully<br>• 9 from the biliary anastomosis<br>—1 from a duct-to-duct anastomosis with T tube<br>—8 from Roux-en-Y anastomoses |
| Biliary strictures | n = 5 (10.6%)<br>• Four managed with revision of Roux-en-Y anastomosis<br>• One managed with stent placement | n = 1 (8.4%; child)<br>• Managed with revision of Roux-en-Y anastomosis | n = 3 (6%)<br>• All had required multiple duct reconstructions (2 grafts with 2 ducts and 1 with 4)<br>• All were managed with operative revision of the existing Roux-en-Y reconstruction |

## Considerations in Pediatric Cases

Any pediatric candidate can be considered for LDLT. With experience, we began to present LDLT as the preferred option for children. Whereas decisions to proceed with LDLT were once slow and tortured, often with a last-minute decision when the child was in extremis, these patients now proceed to expeditious transplantation at the optimal time.

Emergent LDLT has been successfully performed in children.[17] We have performed 10 emergent transplants for fulminant hepatic failure in children, but none in adults. In children with fulminant hepatic failure, the donor is usually a willing parent, and it is this person who gives consent for both his or her own surgery and the child's. In adult-to-adult LDLT, however, the recipient plays a critical part in the decision to use a living donor. An adult with fulminant hepatic failure would usually be unable to participate in this decision. In addition, whereas parents are obvious donors for children, the choice of a donor for an adult is less obvious. For these reasons, and because we have been able to acquire cadaveric donors for status 1 adults, we have not yet had to resort to living donation for adults with fulminant hepatic failure.

## Considerations in Adult Cases

Certain aspects of candidate selection for adult-to-adult LDLT (i.e., diagnostic indication and severity of illness) are controversial. For the most part, diagnostic indications are similar to those in candidates for cadaveric transplants.[9] Current reality, however, dictates that some patients (e.g., with certain forms of cholestatic disease or HCC) have no

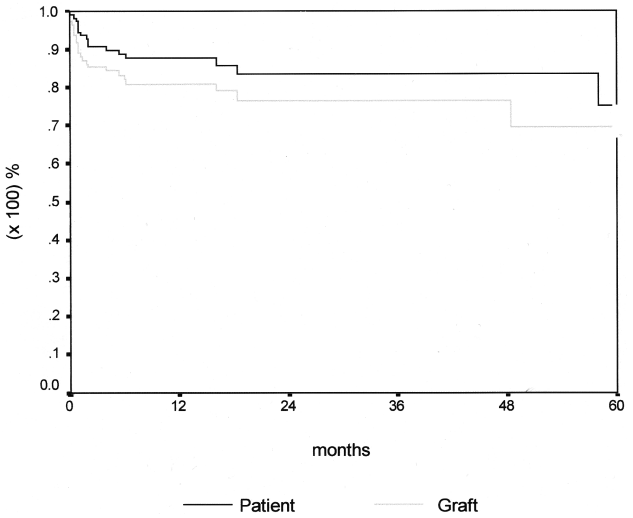


**Figure 3.** Overall actuarial 1-year and 5-year patient and graft survival rates.

realistic chance of receiving a cadaveric liver before they become too ill for transplantation. There is little argument over the use of LDLT in these patients; they represent the largest proportion of candidates in most series.[18]

However, UNOS listing criteria[2] were designed in the context of a severe organ shortage. Use of a scarce cadaver organ in a patient unlikely to survive long term is discouraged. With a living donor, however, the organ shortage becomes irrelevant to a specific recipient, and the decision paradigm changes. Some patients who do not meet UNOS criteria for prioritization, and are thus in effect ruled out from receiving a cadaveric organ, are nevertheless best treated by liver transplant. We offer LDLT to such patients as long as the donor, recipient, and transplant team agree that the risk/benefit ratio is acceptable.[19] With respect to large HCCs, we have been encouraged by our results of selective cadaveric transplantation in patients with tumors larger than 5 cm and by the association of shortened waiting time with improved outcomes.[20] LDLT provides the perfect means to shorten the waiting time and potentially improve results. Our two patients with metastatic malignancies died of tumor recurrence but received dramatic palliation for 1 to 2 years. Whether this outcome justifies the risks to the donor is certainly open to debate.

Also debated is the severity of illness for which LDLT is appropriate. Most programs, including ours, initially hesitated to offer this procedure to our sickest patients with chronic disease (status 2A). With improved understanding of technical issues (in particular, functional graft size, discussed below), application in these sicker patients may be liberalized. For the most part, we have used LDLT in status 2B patients, or in status 3 patients with special indications (e.g., tumor, severe pruritus, retransplantation). In the future, we expect to expand its application to certain status 2A patients while further discouraging its premature application in patients with early disease. Practically, the organ shortage has made it impossible to transplant status 3 patients with cadaveric livers. With LDLT, the benefits of early transplantation must be weighed against the risks to the donor and recipient, especially in patients at high risk for recurrence (e.g., hepatitis C).

## Actual Graft Size Versus Functional Graft Size

In determining whether a donor can provide adequate liver mass with a left or right lobe, it is important to know not just the graft volume but the variables that can reduce its actual functional capacity.[21] Much has been written about the graft size necessary to avoid early graft dysfunction and small-for-size syndrome.[10,22] The generally accepted safe minimum is 40% to 50% of the recipient's normal liver volume, also expressed as a ratio between graft size and recipient size (i.e., the GRWR, which should be $>0.8\%$). Early in our adult experience, when we relied solely on left lobe grafts, we found that in patients with little or no portal hypertension and stable disease, grafts with actual sizes less than 40% provided adequate functional mass. However, when grafts less than 40% were used in less stable patients with hyperdynamic portal flow, the grafts swelled and could not sustain life.[22,23] Clearly, the relationship between actual and functional size was affected by disease severity and portal hemodynamics.

With the initial use of right lobes, we found that suboptimal venous outflow can result in damage to part or all of the graft. When this occurs with severe portal hypertension, even grafts in patients with a GRWR of more than 0.8% may function poorly and develop functional small-for-size syndrome and secondary hepatic artery thrombosis. The transection plane for the right lobe graft must be immediately adjacent to the right border of the middle hepatic vein. This allows for careful dissection and preservation of the segment 5 and 8 veins at their base, and preserves as many intrahepatic collateral veins as possible. In our experience,

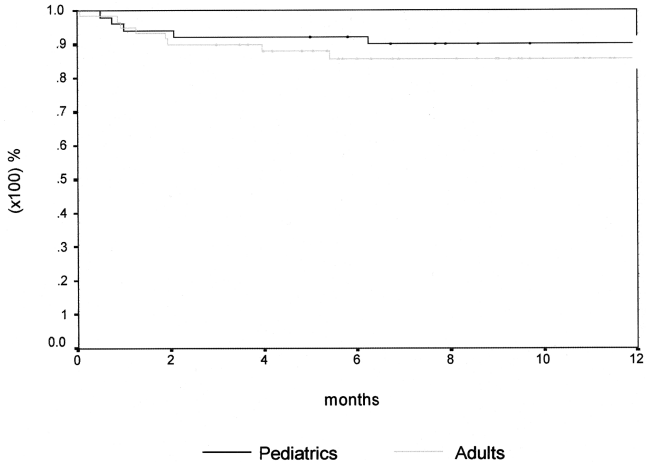


**Figure 4.** Actuarial 1-year patient survival rates in children and adults.

these collateral veins are adequate to prevent functional small-for-size syndrome in most cases. To err on the side of safety and avoid any possibility of venous outflow impairment, when these middle hepatic vein tributaries are larger than 5 mm in diameter, we now routinely provide them with outflow to the middle hepatic vein or the vena cava.

## Donor Outcomes

We have had no donor deaths and only minimal donor complications. Donors had a relatively short length of stay, and only 2 of 109 required reoperation (for intestinal obstruction). Our four aborted donors account for the major morbidity in this series. More thorough donor evaluation could have prevented two of the four; the other two resulted from unexpected intraoperative findings or complications in the recipients. Aborted donor surgery has not been consistently reported in the literature.

Our ability to discuss donor outcomes in the context of national and international experience is limited by the lack of an LDLT registry. In the international experience of approximately 2,500 LDLTs, as the senior author understands it, there have been at least five donor deaths, either reported in the media or discussed at conferences. Only one death has been formally reported.[24,25] Two deaths were in left lateral segment donors, one from a pulmonary embolus and the other possibly related to anesthesia. Three deaths in right lobe donors were related to the technical performance of the surgery or to hepatic dysfunction.

## Recipient Outcomes

LDLT has dramatically changed pediatric liver transplantation, improving survival rates before and after transplant. Since our LDLT program began, we have had higher patient and graft survival rates. LDLT now accounts for 40% of our pediatric transplants.

Complications related to technical issues and to patient and donor selection have diminished over time. We have seen improved results and decreases in hepatic artery thrombosis, portal vein thrombosis, and poor early graft function. Our poor results with left lobes occurred early in our experience, before we fully appreciated the importance of functional graft volume. Others have reported very respectable results using left lobes from living donors,[26–28] and these grafts remain an important option in appropriate recipients. In addition, with an understanding of the necessity of optimal venous outflow and adequate functional graft volume, since May 2000 no patient has required retransplant for inadequate early graft function. Biliary complications continue to occur but usually resolve with prompt treatment. The optimal approach to biliary reconstruction and the management of complications remains to be defined.[29]

LDLT is an important option for patients facing a cadaveric organ shortage and a 10% chance of dying on the waiting list. Our patient survival is equal to our cadaveric results. For patients whose real chance of dying on the waiting list is far greater than 10%, living donors may be the only realistic hope. The donor surgery is safe and can be performed with minimal complications. The success of our living donor program has radically changed our approach to patients with liver failure and unresectable tumors. We expect to perform an increasing number of LDLTs, and we believe that within 3 years 50% of our transplants will involve living donors.

## Acknowledgment

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## DISCUSSION

DR. ABRAHAM SHAKED (Philadelphia, Pennsylvania): Dr. Miller, I enjoyed very much your presentation. We must recognize that the advancement in surgical techniques and understanding the processes of liver regeneration brought the field of liver transplantation to a stage where without a doubt segmental transplantation is possible. You have shown us the outstanding results where surgery, at least with the right lobe, is comparable with cadaveric transplantation.

I have two questions for you. The first is related to indication for transplantation. Now that we have an "unlimited" number of livers available for donors, does it mean that the indication for transplantation is changing? Let me give you an example. We never did patients with large hepatocellular carcinoma. We did not do patients with large cholangiocarcinoma. Now these patients are coming to us with their own donors and telling us that they are willing to undergo these procedures even though the success rate is low. Should we accept those? Should we modify our criteria for recipient selection? Do we have to have any criteria for recipient selection at all if they bring their own donors? It is not a precious commodity anymore.

The second question is related to data that I saw in your manuscript and you did not touch it. The fact is that you have a very interesting dichotomy between the adults and the children in terms of rejection rate. In the adults, the rejection rate in the living studies was about 18% whereas in the children it was 32%. Now, 32% is more similar to cadaveric. We also noticed decreased rates of rejection in the adults with living donors. The only variable that is different between the two (both are living donations), is the fact that in the children the liver does not have to regenerate while in adult it does have to regenerate. Does regeneration decrease the rate of rejection?

PRESENTER DR. CHARLES M. MILLER (New York, New York): Dr. Shaked, I appreciate your comments. In terms of expanding recipient criteria, the criteria for cadaveric organs was made in a severe organ shortage crisis and we have had to systematically triage patients. For those patients with his or her own living donor, there is no shortage and triage may no longer be appropriate.

On the other hand, the risks and benefits, the issues of recurrence in cases of tumors, have to be clearly explained. The way we do it, is to set up a donor, recipient, and transplant professional team that fully understands and agrees on the risks and benefits before proceeding.

In terms of your question about rejection, I really don't know. The adult experience is more recent. And since we began, we have been using monoclonal IL-2 antibody induction. This may be a partial explanation.

Your question about regeneration and alloreactivity islet is fascinating, and would be something that I think you could probably answer better than I.

DR. GORAN B. KLINTMALM (Dallas, Texas): The use of living donors was once the means to make kidney transplantation develop. Only later did cadaveric donors become the main source of organs.

In liver transplantation the situation is reversed. The specialty established using cadaver donors. Four years ago we heard at this Association meeting the first experience using living donors for adult recipients. In only a couple of years this technology has changed liver transplantation.

Dr. Miller and his colleagues at Mount Sinai have delivered their large experience using liver donors for children and adults. They have a unique experience allowing them to advise us all.

Even with the prodigious experience we have at Baylor with liver and biliary surgery and with liver transplantation, we have found that adult-to-adult liver transplantation is filled with dangers. However, it is noted that most of the exploitation of this technique is taking place in transplant programs with only modest experience.

I have a few questions for Dr. Miller. How do they deal with the ethical question of subjecting the donors to this huge and potentially dangerous operation? Second, what is the true morbidity and mortality of donors in the United States and not in an expert program like yours? Thirdly, is there any way for us to ensure that the expansion of this technique is done with the safety of the donor in mind and not for the notoriety of the institution or because of the competition for cadaver organs?

DR. CHARLES M. MILLER: Thank you, Dr. Klintmalm. I don't know exactly what the morbidity and mortality of this operation is in the United States. I know of at least four deaths because I have had personal communications with the surgeons involved in these cases. I guess that the denominator for the world experience is about 2,500 or 3,000 donors. I know of a fifth death that was reported in the French newspapers. There is also morbidity; this is a large operation, and it takes rigorous efforts to minimize it.

We don't have a registry yet. The American Society of Transplant Surgeons have advocated and are beginning to set up a registry for living donors in liver transplantation. This will be very valuable, especially if people report their experience. How to get people to report their experience fully and honestly is something that I pray happens, but I am not certain that it will. It is certainly the best thing to do in any technology that is evolving as rapidly as this, and hopefully I will be able to give you an better answer next year.

DR. CHRISTOPH BROELSCH (Essen, Germany): Exactly ten years ago the first report on living related liver transplant was presented to this Association here. Since then a dramatic evolution has taken place with live donors today ending up with less liver than the recipient, leading to the death of three donors in Europe, including the United States experience a total of 2,500 cases of live donor liver transplants have been performed until now.

The benefit of the initial procedure was exclusively for small children who were dying on the waiting list. With the application of splits, cadaveric transplants, and live liver donors, mortality of children on the waiting list has virtually ceased. Presently it is the adult candidates who die at a high level of percentage. Their mortality will increase dramatically unless we find ways to provide more organs or part of organs. Dr. Miller's group needs to be complimented for their approach to gradually employ all feasible procedures to increase organ availability.

The last step was the employment of full liver lobes, which presents a major operation for the donor. During the last year, performing some 120 transplants in your institution, an equal number of patients died on your waiting list. I understand patients are being offered both cadaveric as well as living donor options, but how do the potential donors perceive this

information, as pressure or coercion or as relief or even redemption from a very pressing problem? Ethicists always postulate an uncoerced decision of adults in a social setting like this. Is such a thing existing?

My second question relates to the potential broadening indications that Dr. Shaked has already mentioned, the so-called extended indications. Society apparently fails to provide sufficient cadaveric donor organs while societal altruism favors donations in certain settings irrespective of the long-term outcome. It is a constant fight, society versus the individual.

Society limits organ allocation to definite indications quite rightly so — with limited resources. But what about those who simply want to live on for some years, like when cancer developed in their livers? Or even in the very late stage of their diseases when they might even die on the operating table, should they benefit from an available donor organ from a relative? I would ask that question.

And the last question relates to the decreasing activity in cadaveric organ splitting. Is the living donor operation done in daylight surgery, well prepared, more compelling, more safe for the recipient than a split procedure done at night in outside operating rooms with uncertain success?

There is thus far a higher complication rate with cadaveric splitting. Do patients consent to this procedure rather than do they prefer live organ donation, at least in your institution? It is our experience that they actually vote much more in favor of live organ donation than receiving a cadaveric split.

There is much more to discuss on your excellent paper, Dr. Miller, particularly surgical techniques and donor safety aspects, but it is more important to note that you have established a sensitive balance between cadaveric transplants and living transplants. Because of our western society and civilization, transplant centers should provide all types of organ transplants and should not be driven by ambitious preference.

DR. CHARLES M. MILLER: Dr. Broelsch, thank you for the privilege of having you discuss this paper. Your contributions were pioneering.

With respect to coercion, the consent process is designed for repeated conversations and we give patients and donors an "opt-out" where we can create a little white lie so that the potential donor doesn't suffer any kind of embarrassment if they decide to back out.

We now present living donation as a good option. We didn't in the initial stages of our pediatric transplantation program and we lost out on most of the benefits. What people found themselves doing was waiting and waiting and waiting until the child got very sick, and then at the last stage deciding to donate. We lost out on major opportunities to do cases while the recipient was in a better state of health and we were defeating the purpose. So we took a positive, proactive approach where we have many people discuss the options with them, and they have a donor advocate and they can opt out at any time.

In regard to extended indications, I think we are approaching that in the same gradual progressive way that we approached the whole evolution for the program. With respect to hepatocellular carcinoma, many patients die while waiting and their tumors are growing. Probably the best thing we have to cure hepatocellular carcinoma is a prompt transplant. And living donation provides that option.

There has been a decreased activity in cadaveric splits. I hope that further understanding of segmental lobar transplantation through living donors will provide the same impetus for left/right lobe splits as the left lateral segment living donor did for the left lateral segment/right trisegmental split that has been so successful in many people's hands.

DR. LESLIE H. BLUMGART (New York, New York): Thank you very much, Dr. Miller, for a very fine presentation. I should like, however, to sound a note of caution and ask for your comment. This relates to tumor and the use of live donor liver transplantation cancer in adults. There are particular risks utilizing the right liver.

I can just about accept the concept for patients with small hepatocellular carcinoma but find very considerable difficulty in accepting it ethically for patients with large lesions as has been suggested, and indeed even for patients with small lesions and Childs A liver function. I very much agree with Russell Strong's recent statement that the first reaction on discovery of a small liver tumor should be resection and not an automatic move to transplantation.

So my question really relates principally as to whether the transplant community is entirely happy with the ethics of using live related donor transplantation for cancer in adults and whether it is justified to put the donor at risk in such situations.

One other point, and I see Roger Jenkins is about to ask a question, in a publication just about one week ago, Dr. Jenkins' group in Boston reported a morbidity, including all complications, of about 50-70% and that many donor livers had to be rejected because of anatomic abnormality. I noticed you had very few donor rejections because of vascular abnormality or other anatomical variations, this despite the fact that you were doing quite detailed investigations. Perhaps you had just not mentioned it, but this does not match the recent publication from Boston and I wonder whether you would comment on that.

DR. CHARLES M. MILLER: Thank you, Dr. Blumgart. I know your concerns, and I think we agree more than we disagree. I think many patients with isolated single lesions in the CHILDS A class may be approached for resection. But it is really important to remember that patients with hepatitis C and other forms of cirrhosis have tumors that are rarely unifocal and oftentimes recurs after resection. Transplantation after it has recurred post-resection is a less good option.

In large tumors I think it really depends on how large it is. We have had very gratifying results in a very carefully analyzed series of patients with tumors between 5 and 7 centimeters with about a 50-55% patient survival and a 45% recurrence-free survival at five years. I think if we can apply this technology to that set of patients in an expeditious way, it may even improve the results more.

We have actually excluded only one donor on imaging. He had a portal vein that gave three separate branches to the right lobe and then coursed through the right lobe, and we ruled him out. We have done three cases with double portal veins reconstructed with either iliac vein grafts or with portal vein from the recipient. There are in fact very few anatomical contraindications to proceeding.

DR. ROGER L. JENKINS (Burlington, Massachusetts): Dr. Miller, congratulations on your work; in fact, your entire team's work. Anybody involved in this knows that this is a huge team effort. I would be curious to know what you think is a proper component of the surgical portion of the team and what sort of preparation they should go through.

The impact of adult live donor transplantation is such that it is becoming a far more important component for all of us. In fact, this year so far, live donor liver transplantation has represented 50% of our volume.

Two quick questions. One of them is, for the vascular grafts that you use on the middle hepatic vein, do they stay open? If so, how long? Do they need to stay open for more than 24 to 48 hours? Most of the ones that we have done have occluded, and yet we have not seen any untoward events. Finally, for those extended indications for transplantation where patients may not be UNOS acceptable candidates. If their graft fails and the only salvation for them is a cadaveric transplant, do you list them for retransplantation? At that point they dip into the scarce donor pool.

DR. CHARLES M. MILLER: Those are good questions, Dr. Jenkins.

With regard to the surgical preparation of the team. We have five surgeons who are capable of performing either the donor or the recipient operation and basically have two senior surgeons on the donor and two senior surgeons on the recipient, along with some fellows. We do these operations simultaneously, and try to provide an additional level of expertise in these cases.

The segment 5 and 8 vein grafts often don't stay open, and I don't think they need to. Because there are collaterals, I think you probably only need these vein grafts in 10% of the cases. It is just that I haven't discovered how to know when yet. So it is a little like a belt and suspenders approach.

Collaterals, if they are not open initially, probably do open between the middle hepatic vein branches and the right hepatic vein and over a period of days these new vein grafts may close. However, if you don't give these livers adequate outflow early on, you will damage the graft.

And finally, most of the patients who may not be UNOS candidates actually do meet minimal listing criteria, it is just that they can't be prioritized in any reasonable way to have a practical chance to get over it. So yes, we do relist them. And actually our retransplant rate now has fallen to such a low level for early graft failure that it is really not an issue.